Remarks

Claims 1 and 3-169 are currently pending in this application. Claims 3, 9, 10, 13-67, and 70-169 are withdrawn from consideration as being drawn to non-elected inventions. Claim 11 has been amended so that it does not depend on a non-elected claim. The rejections set forth in the Office Action Mailed September 26, 2005 are traversed by Applicants' arguments set forth below.

1. Claim Rejections - 35 USC §103

Claims 1, 4-5, 11-12, and 69 stand rejected under 35 USC §103(a) as allegedly being unpatentable over Bagshawe *et al.* (US Patent 6,299,876) in view of Knecht *et al.* (WO 01/88106).

Bagshawe *et al.* teach methods for sensitizing tumor cells to cytotoxic agents by conjugating enzymes that inactivate anti-cytotoxic agents with specific antibodies that target specific tumor cells. The methods of Bagshawe *et al.* require an enzyme-antibody conjugate that targets a tumor cell, wherein the enzyme inactivates some substance in the cell that can inhibit the effect of a cytotoxic agent. As an example, Bagshawe *et al.* teach that carboxypeptidase G2 inactivates folinic acid at tumor sites to leave the tumor cells unprotected against trimetrexate (col. 12, lines 39-42). Bagshawe *et al.* also discuss the possibility of using enzymes that convert prodrugs to active drugs, but only in the presence of an enzyme that inactivates some cytotoxic substance in the target cell (col. 12, lines 45-50), or when the enzyme itself can also inactivate some cytotoxic substance in the target cell (col. 12, lines 37-39). Bagshawe *et al.*, therefore, do not teach improving the activation of a cytotoxic agent without inhibiting anti-cytotoxic substances within a tumor cell. In addition, as pointed out by the Action, Bagshawe *et al.* do not teach modified deoxycytidine kinase for any purpose.

The Action alleges that Knecht *et al.* teach that modified deoxycytidine kinase increases enzymatic activity towards nucleoside analogs, citing page 4, lines 3-7. However, Applicants respectfully submit that Knecht *et al.* only disclose the effects of deoxyribonucleoside kinase variants, and not deoxycytidine kinase as alleged in the

Action. Knecht *et al.* do not disclose the effects of any modified human deoxycytidine kinases. In particular, Knecht *et al.* do not demonstrate that modified deoxycytidine kinase can convert a prodrug into a cytotoxic drug. Indeed, the only experiments in Knecht *et al.* involve deoxyribonucleoside kinase variants.

The Action asserts that it would have been obvious to one of ordinary skill in the art to make the enzyme-antibody conjugate of the Bagshawe *et al.* comprising modified deoxycytidine kinase of Knecht *et al.* for cancer treatment. Applicants submit, however, that the enzyme-conjugates taught by Bagshawe *et al.* comprise inhibitors of anti-cytotoxic agents, while the enzyme-conjugates of the instant invention comprise modified deoxycytidine kinase that can activate a chemotherapeutic agent. Applicants further submit that the teachings of Knecht *et al.* do not remedy the deficiencies of Bagshawe *et al.*, because Knecht *et al.* do not disclose activation of a chemotherapeutic agent by modified deoxycytidine kinases. Therefore, these two references do not render the instant claims obvious, because Bagshawe *et al.* teach methods that comprise using inhibitors of anti-cytotoxic agents and Knecht *et al.* do not teach conversion of a prodrug into a cytotoxic drug by modified deoxycytidine kinases. Consequently, Applicants respectfully request that this ground of rejection be withdrawn.

2. Claim Rejections - 35 USC §103

Claims 1, 4-8, and 11-12 stand rejected under 35 USC §103(a) as allegedly being unpatentable over Bagshawe *et al.* (US Patent 6,299,876) and Knecht *et al.* (WO 01/88106) in view of Kossman *et al.* (*Clin Can Res.* 1999, Vol. 5, pages 2748-55).

Kossman *et al.* teach the effects of the humanized M195 antibody (HuM195) in patients with acute myeloid leukemia. Kossman *et al.* do not teach antibody-conjugates comprising HuM195. As discussed above, neither Bagshawe *et al.* nor Knecht *et al.* teach or suggest that modified deoxycytidine kinases can activate a chemotherapeutic agent in a specific tumor cell when delivered to the cell as an enzyme-antibody conjugate. Likewise, Kossman *et al.* does not teach or suggest that modified deoxycytidine kinases can activate a chemotherapeutic agent in a specific tumor cell when delivered to the cell as an enzyme-antibody conjugate. Applicants submit,

therefore, that these three references, even in combination, do not provide any teaching or suggestion that the HuM195 antibody could or should be conjugated with modified deoxycytidine kinases to activate a chemotherapeutic agent in a tumor cell. Consequently, Applicants respectfully request that this ground of rejection be withdrawn.

Conclusion

Applicants respectfully contend that all conditions of patentability are met in the pending claims as amended or as originally presented. Allowance of the claims is thereby respectfully solicited.

If there are any questions or comments regarding this Response or application, the Examiner is encouraged to contact the undersigned representative as indicated below at 312-913-0001.

Respectfully submitted,
McDonnell Boehnen Hulbert & Berghoff LLP

Date: December 27, 2005

By: _____
Jason J. Derry
Reg. No. 50,692